IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Abraham J. Domb and Joseph S. Wolnerman

Serial No.: 10/083,413 Art Unit: 1655

Filed: February 27, 2002 Examiner: Flood, Michele C.

For: *ABSORBABLE SOLID COMPOSITIONS FOR TOPICAL TREATMENT OF ORAL MUCOSAL DISORDERS*

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

The applicants respectfully request review of the final rejection in the above-identified application for the reasons stated below.

The claims are directed to a solid, self-bioadhesive composition for topical application to oral mucosal tissue to which it adheres. The composition comprises a bioactive amount of at least one herbal active agent: a bioactive herb, herbal extract, tincture, essential oil, or mixture thereof; or an analgesic, anti-inflammatory, antihistamine, antigen, steroid other than an anti-inflammatory, antimicrobial drug, vitamin, enzyme, antipyretic, antimalarial, antiulcer drug, peptide, or combination thereof, *wherein the agent is present in a homeopathic amount*. The composition further comprises a pharmaceutically acceptable solid bioadhesive carrier present in

an amount from about 40 to about 99 percent by weight of the whole composition. Claims 4, 6, 7, 8, 9, 10, 11, 19, 20, and 25 are specific to herbal formulations.

These compositions, and in particular those formed into the disks of claims 2 and 3, are prepared by *compression molding* rather than solvent casting. Solvent casting typically requires drying at elevated temperatures in order to remove the solvent. Herbal extracts and essential oils can be extremely sensitive to heat and can degrade at elevated temperatures thereby destroying their therapeutic effectiveness. The bioadhesive carrier is a material that attaches to mucosal tissue upon hydration. The carrier must be capable of maintaining adhesion in moist or wet environments *in vivo*. The final composition is self-adhesive in that it attaches to the site of interest without the need to reinforce its attachment by way of another adhesive which is applied to a backing. The composition should adhere to mucosal tissue for at least 30 minutes, preferably from about 1 to about 24 hours, more preferably from about 3 to about 10 hours, as defined by claims 2 and 3.

35 U.S.C. § 112, First Paragraph

Claims 1-4, 6-12, 14-17, and 19-26 were rejected under 35 U.S.C. § 112, first paragraph, because the claims are allegedly not enabled for a therapeutically effective amount of a homeopathic agent. Specifically, the Examiner alleges at that the time the application was filed, the state of the art did not fully support the incorporation of homeopathic agents or homeopathic amounts of active agents into pharmaceutical compositions intended for administration to

patients. The Examiner points to the website www.quackwatch.com and an article by Dr. Stephan Barrett.

It is believed that the examiner has indicated on page 7 that once the alleged new matter was replaced with the language "a solid, self-bioadhesive composition for topical application that adheres to oral mucosal tissue comprising a therapeutically effective amount of " the listed agents, the lack of enablement rejection would be withdrawn. Applicants would be willing to make this amendment. To facilitate prosecution.

In response to the statement that applicants have failed to provide a working example, the examiner's attention is again drawn to page 36 of the application as filed, which fully supports enablement of composition as defined by the amended claim.

The term "homeopathic" is well known to those skilled in the art. Homeopathic medicines, tinctures and powders are commercially available and widely used. So much so that states have enacted definitions of "homeopathic", copies of which were previously submitted to further demonstrate that the meaning of this term was well known and understood by those skilled in the art, and not considered "quackery" as indicated by the examiner. Note that laws governing treatment of patients with homeopathic medicine were enacted in numerous states between 1992 and 1995, long before this application was filed. Moreover, the examiner has failed to provide any evidence, only argument based on an obscure website, nothing that can rebut the statutory presumption that such medicines and use in treatment thereof was known,

regulated under state law, and accepted generally. Indeed, the prior art cited by the examiner demonstrates that homeopathic compositions generally are well known.

35 U.S.C. § 112, Second Paragraph

The Examiner alleges that claims 15-17 and 19-21 are indefinite. Specifically, the Examiner alleges that the phrase "further comprising a non-herbal active agent" is indefinite since claim 1 defines the active agent as an herbal agent, a homeopathic agent, or a drug. In order to facilitate prosecution, the applicants are willing to amend claim 1 to define the active agent as selected from the group consisting of an herbal agent, a homeopathic agent, a drug, or combinations thereof and to cancel claim 15. Claims 16 and 17 would be amended to depend from claim 1. The Examiner also alleges that claim 19 lacks antecedent basis. Applicants are willing to amend claims as required to moot this rejection.

Should the case be otherwise allowable, an amendment to make the changes recommended by the examiner on page 8 would be submitted.

Rejections Under 35 U.S.C. § 102 and 103

Claims 1-3, 15-17, 22-24, 26, 27, and 38 were rejected under 35 U.S.C. 102(b) as disclosed by U.S. Patent No. 4,226,848 to Nagai, et al. Claims 1-4, 6, 15-17, 22-24, 26, 27 and 38 were rejected under 102(b) as disclosed by U.S. Patent No.4,772,470 to Inoue, et al. Claims 1-4, 6-12, 15-17, 19, 22-27 and 38 were rejected under 35 U.S.C. 103 as obvious over Inoue, et al. in combination with U.S. Patent No. 5,939,050 to Iyer, et al. and U.S. Patent No. 6,197,305 to

Friedman, et al. along with Lawless, The Illustrated Encyclopedia of Essential Oils, Element Books, 1995 ("Lawless").

Inoue describes films, not solid colloidal forms (pages 12, 14) or compressed tablets, and not disks as defined by claims 2 and 3. Inoue does not disclose administering homeopathic amounts of active agents. Inoue mixes polycarboxylic acid polymers for adhesion and polyvinyl acetate for swelling (because it is a gel, not a tablet) (Col. 4) and avoid the effects of dissolution and release of polycaboxylic acids (col. 5). Significantly greater amounts of carboxylic acid polymer is required for long term adhesion of tablets as compared to films.

Nagai, et al. discloses a controlled release formulation which can contain 5-50% acrylic acid polymer and must contain 50-95% cellulose ether. Applicants do not require cellulose ether and do require greater amounts of a polycarboxylic acid polymer for bioadhesion. Nagai does not disclose tablets but granules or a powder when high adhesion is required (col. 7). Nagai teaches away from use of polycarboxylic acid polymers alone (bottom of col. 3). There is no disclosure of homeopathic amounts of active agent.

U.S. Patent No. 5,939,050 to Iyer *et al.* ("Iyer") describes antimicrobial compositions comprising at least two antimicrobial agents which exhibit reduced MIC values relative to the MIC values for the agents making up the combination when measured alone (abstract). Iyer does not disclose a solid, self-bioadhesive tablet formulation for topical application that adheres to the oral mucosal tissue. As noted at col. 7, lines 16-27 and lines 53-61, these formulations are oral rinses, mouth wases or cleansers.

Friedman does not disclose a solid, self-bioadhesive composition for topical application that adheres to the oral mucosal tissue. The formulations are not bioadhesive. Ingredients such as those at col. 7 are either hydrophobic (such as beeswax) or liquid (glycerin and oil) or contain detergent (such as sodium lauryl sulfate). Table 3 is liquid, not solid. Table 4 is a gel primarily of polyethylene glycol, which is not bioadhesive alone. Table 7 is similar. Tables 5 and 6 are hydrophobic skin cream. Example 10 contains similar examples to the other examples.

Lawless discloses that the essential oil of lemon contains approximately 70% limonene as well as sabinene, myrcene, and pinenes (page 120). Lawless does not disclose a self-bioadhesive composition for topical application that adheres to oral mucosal tissue, nor a homeopathic amount.

For the foregoing reasons, Appellant submits that claims 1-4, 6-12, 14-26, and 38 are patentable.

Respectfully submitted,

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